

### REMARKS

Claim 42 has been amended to remove C (natural pyrimidine). Claims 45 and 49 have been amended to correct their dependency on claims 44 and 48, respectively.

#### Rejection of Claims 20-21, 42-44 and 48 under 35 U.S.C. §103(a): Chaix and Schwartz

Claims 20-21, 42-44 and 48 are rejected as being obvious over Chaix et al and Schwartz. Schwartz is relied upon as disclosing immunostimulatory oligonucleotide sequences comprising a CpG dinucleotide wherein the cytosine is modified. Chaix is relied upon as teaching oligonucleotides comprising a 3'-3' linker and two accessible 5' ends. The asserted motivation to combine the references is that Chaix teaches that the 3'-3' linkage results in a marked increase in oligonucleotide stability, thus one would be motivated to incorporate the 3'-3' linkage of Chaix into the immunostimulatory oligonucleotide of Schwartz to stabilize the oligonucleotide against nucleolytic degradation. It is asserted that there would be a reasonable expectation of success "given the underlying techniques are commonly used and widely known". (Office Action at page 5). Applicants respectfully disagree with this latter assertion.

The error in this statement is because the technique of linking two oligonucleotides at their 3' ends was unknown and previously never used in the art of oligonucleotide based immunostimulatory compounds. Before Applicants' disclosure, nobody knew the roles of either end of the oligonucleotide in such oligonucleotide based immunostimulatory compounds. Part of Applicants' invention was the recognition that immunostimulatory activity requires an accessible 5' end, but not an accessible 3' end. It is solely Applicants' specification that teaches that making the 3' ends of such compounds inaccessible is not fatal to their activity as immunostimulatory compounds. Thus, Applicants own teaching is being used to provide the requisite expectation of success for obviousness. This is impermissible hindsight. Accordingly, Applicants respectfully request that this rejection be withdrawn.

#### Rejection of Claims 45 and 49 under 35 U.S.C. §112, second paragraph

Claims 45 and 49 are rejected as being indefinite for being dependent on canceled claims 04 and 08, respectively. Applicants thank the Examiner for pointing out this inadvertent error. Claims 45 and 49 have been amended to correct this error, specifying that they are dependent on claims 44 and 48, respectively. This rejection also notes that "at least 5-hydroxymethylcytosine

and 5methylcytosine occur naturally by way of oxidative damage to phage and E. coli DNA.” However, it is unclear whether this is intended to be a further basis for the rejection. At any rate, in the specification as filed, at page 13, lines 2-4, the term “non-natural pyrimidine nucleoside; when used to describe structure I, means “not cytidine or deoxycytidine”. Applicants respectfully request that this rejection be withdrawn.

Rejection of Claims 42, 43, 46, 47 50 and 51 under 35 U.S.C. §103(a): Schwartz, (Chaix) and Jennings

Schwartz is relied upon as previously. During a telephonic interview with the Examiner on November 17, 2008, it was clarified that Chaix was intended to be included in this rejection and to be relied upon as previously. Jennings is relied upon as teaching “that nucleoside derivatives, including arabinose, are resistant to nuclease attack.” The rejection further asserts that “There would have been a reasonable expectation of success given the underlying techniques are widely known and commonly used.”

Applicants reiterate their previous reply with respect to Chaix and Schwartz.

In addition, before Applicants’ disclosure the technique of incorporating non-naturally occurring sugars in a CG dinucleotide was not known and never used in the art of oligonucleotide based immunostimulatory compounds. Only Applicants’ own specification teaches that such oligonucleotide based immunostimulatory compounds having such modified sugars in a CG dinucleotide retain immunostimulatory activity. Thus, it is Applicants’ own specification that is being used to provide the requisite expectation of success for obviousness, which is impermissible hindsight.

Accordingly, Applicants respectfully request that this rejection be withdrawn.

Double Patenting

Claims 42-45, 48 and 49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 7262286 in view of Chaix. Applicants respectfully traverse this rejection on grounds that Chaix does not provide the requisite expectation of success for obviousness, as discussed in detail in the above reply to the obviousness rejection over Chaix and Schwartz. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Allowable subject matter

Applicants acknowledge that claim 41 is objected to as being dependent on a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

**CONCLUSION**

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner believes that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned attorney at 781-933-6630.

Respectfully submitted,

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